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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,515	03/17/2006	Yuji Hoyano	Q93797	4754

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EXAMINER	
BAEK, BONG-SOOK	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,515	HOYANO ET AL.	
	Examiner	Art Unit	
	BONG-SOOK BAEK	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,10,12,17 and 26-33* is/are pending in the application.

4a) Of the above claim(s) *10,12,17 and 26-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

The amendment filed on February 17, 2009 is acknowledged. Claims 1, 4, 10, 12, 17, and 26-33 are currently pending and claims 10, 12, 17, and 26-33 have been withdrawn. Claims 1 and 4 are under examination in the instant office action.

Applicants' arguments, filed on February 17, 2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. Responses are limited to Applicants' arguments relevant to either reiterated or newly applied rejections.

The following rejection is maintained for reasons of record and the followings

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US patent 6,541,488 B1 (Issue date: 4/1/2003) in view of WO 02/28827 A1 (publication date: 4/11/2002), as evidenced by an English translation of WO 02/028827 A1 (part1 and part2), publication date: 11/04/2002. A copy of PCT application WO/2002/028827 is not supplied since applicant has a copy.

The instant invention is drawn to a composition comprising an anti-platelet agent (elected species: cilostazol) in combination with a 5-amidino-2- hydroxybenzene sulfonamide derivative (elected species: [4-[2-(5-amidino-2-hydroxybenzenesulfonylamino)ethyl]- 2'-methanesulfonylbiphenyl-3-yloxy]acetic acid).

US patent 6,541,488 B1 teaches a pharmaceutical composition containing one or more direct or indirect selective inhibitors of activated blood coagulation factor X (factor Xa) in combination with an anti-platelet aggregation agent such as cilostazol for the treatment of thromboembolic arterial diseases (abstract; column 2, line 16-line 33; and column 5, lines 5-31). However, it does not specifically teach 5-amidino-2- hydroxybenzene sulfonamide derivatives as a direct or indirect selective inhibitor of Xa.

WO/2002/028827 teaches that a 5-amidino-2-hydroxybenzene-sulfonamide derivative has a potent and selective inhibitory activity against factor Xa and is useful as preventive or therapeutic drugs for diseases whose onset is related to factor Xa such as thrombosis and

embolism (abstract and p24, lines 8-24 of translation-part 1 of WO/2002/028827) and names the elected species of 5-amidino-2-hydroxybenzene-sulfonamide derivatives, [4-[2-(5-amidino-2-hydroxybenzenesulfonylamino)ethyl]- 2'-methanesulfonylbiphenyl-3-yloxy] acetic acid as a preferable embodiment (claim 9)

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine an anti-platelet agent and a 5-amidino-2-hydroxybenzene-sulfonamide derivative each of which is taught by the prior art to be effective for inhibiting thrombosis and/or embolism in order to get a composition comprising both agents to be used for the very same purpose. See *In re Kerkhoven*, 626 F. 2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In addition, US 6,541,488 B1 provides motivation since it teaches synergistic effect of combination therapy of an anti-platelet agent with other direct or indirect selective inhibitors of (factor Xa) on treating thromboembolic diseases.

Response to Applicants' arguments:

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, US patent 6,541,488 B1 teaches a pharmaceutical composition containing one or more direct or indirect selective inhibitors of activated blood coagulation factor X (factor Xa) in combination with an anti-platelet aggregation agent for the treatment of thromboembolic arterial diseases and WO/2002/028827 teaches the elected compound (4-[2-(5-amidino-2-hydroxybenzenesulfonylamino)ethyl]- 2'-methanesulfonylbiphenyl-3-yloxy] acetic acid), which has a potent and selective inhibitory activity against factor Xa and is useful as preventive or therapeutic drugs for diseases such as thrombosis and embolism. Thus, as stated in the previous action mailed on 8/18/2008, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine an anti-platelet agent and a 5-amidino-2-hydroxybenzene-sulfonamide derivative each of which is taught by the prior art to be effective for inhibiting thrombosis and/or embolism in order to get a composition comprising both agents to be used for the very same purpose. In addition, US 6,541,488 B1 provides motivation since it teaches synergistic effect of combination therapy of an anti-platelet agent with other direct or indirect selective inhibitors of (factor Xa) on treating thromboembolic diseases. "It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition to be used for the very same purpose.....The idea of combining them flow logically from their having been individually taught in the prior art." See *In re Kerkhoven*, 626 F. 2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In response to applicant's argument that the direct factor Xa inhibitor taught by US patent 6,541,488 B1 have entirely different chemical structures from the claimed direct factor Xa inhibitor, they may have different chemical structure, however they are functional equivalent as a

direct factor Xa inhibitor, thus it would be prima facie obvious to substitute one direct factor Xa inhibitor taught by US patent 6,541,488 B1 with another direct factor Xa inhibitor taught by WO/2002/028827.

With regard to selection to the anti-platelet agents, the reference clearly lists cilostazol as an anti-platelet aggregation agent along with aspirin, which can be used in combination with a direct or indirect factor Xa inhibitor. Thus, it would be prima facie obvious to select any anti-platelet aggregation listed in the reference although the preferable embodiments disclosed in the reference used aspirin or an antagonist of glycoprotein IIb/IIIa in combination with an indirect factor Xa inhibitor.

With regard to alleged superior effects on inhibiting the thrombus formation and improving the hypercoagulable state, the alleged superior effect is not claimed as a range or by functional language, so Applicant's possible unexpected result is not commensurate with the scope of the claimed invention. In addition, a mere statement of unexpected result is not considered to be persuasive without supporting factual evidence.

Conclusion

No claims are allowed.

No new ground(s) of rejection has been presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 9:00-6:00 Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614
Bbs

BONG-SOOK BAEK
Examiner, Art Unit 1614